



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
NATIONAL HEALTH AND ENVIRONMENTAL EFFECTS
RESEARCH LABORATORY
RESEARCH TRIANGLE PARK, NC 27711

OFFICE OF
RESEARCH AND DEVELOPMENT

CROFTON, 1998 i

MEMORANDUM

Date: 18 October 1998 (revised 10 November 1998 and 23 November 1998)

Subject: Analysis and Graphics of Thyroid Hormone Data from the Mouse
Immunotoxicology Study

From: Kevin M. Crofton

Neurotoxicology Division, MD-74B
National Health Effects and Environmental Research Laboratory

To: Annie Jarabek
National Center for Environmental Assessment

Attached is the statistical analysis of the hormone data from the Mouse Immunotoxicology Study conducted by Keil et al. (1998). I have attached a description of how the analyses were done and some summary graphs.

The revision of 11/23/98 incorporates your last corrective comments and also contains an additional explanation of how the data were obtained (including email messages in Appendix 1).

Note: The raw data used in this analysis is not the same as that found in either the first (08/01/98) or second (09/30/98) report submitted to the Agency by Dr. Keil. Neither report contains all the data. The data used herein was compiled from both reports and also from files directly emailed to you and I from Dr. Keil. I had Dr. Keil review and approve the data that I used for this analysis (see Appendix 1).

Analyses of Thyroid Hormone and Thyrotrophin Data from the MUSC Mouse Perchlorate Immunotoxicology Study

Summary: The report by Keil et al. (1998) contains thyroid hormone and thyrotrophin data from 14- and 90-day exposures to ammonium perchlorate in B6C3F1 mice. The following is a statistical analysis of the thyroid and pituitary hormone data (T4, thyroxine; TSH, thyroid stimulating hormone) found in that report. There was not analysis of triiodothyronine (T3) in this report. Results of these re-analyses are different from those stated in the report. The re-analysis of the data indicates a statistically significant time- and dosage-dependent decrease in T4 following perchlorate exposure; after 14 days of exposure at 30 mg/kg/day, and after 90 days of exposure at 1, 3, and 30 mg/kg/day. The decrease in T4 recovered to control values 30 days after cessation of exposure (day 120). The NOEL for the effects of perchlorate on T4 in the mouse was 0.1 mg/kg/day. There was no statistical significance of any dose of perchlorate on TSH.

Data: All data were supplied in Excel spreadsheets by Dr. Deborah Keil. Data were exported as ascii files for analyses by SAS. Data for dependent measures (T4 and TSH) were subjected to separate analyses. T4 data were analyzed with a two-way ANOVA, with Duration (14, 90 and 120 days) and Treatment (dose) as the independent between-subjects variables. TSH data were analyzed with a two-way ANOVA with Duration (90 and 120 days) and Treatment (dose) as the independent between-subjects variables. Mean contrasts were performed using Tukey's Studentized Range (HSD) Test. To correct for multiple comparisons (i.e., separate analyses for T4 and TSH) the acceptable alpha for significance (for all interaction main effects tests) was corrected to 0.035 (alpha of 0.05 divided by the square root of the number of dependent variables). SAS analysis code and output are attached (Appendix 2).

Data Analysis - Results:

Total Serum Thyroxine (T4): There was a significant Duration*Treatment interaction and significant main effects of Treatment for the 14- and 90-day data. There was no main effect of Treatment for the 120-day data. The T4 data are plotted in Figure 1.

Thyroid Stimulating Hormone (TSH): There was no significant interaction of Duration and Treatment, nor was there a main effect of Treatment. Data are plotted in Figure 2.

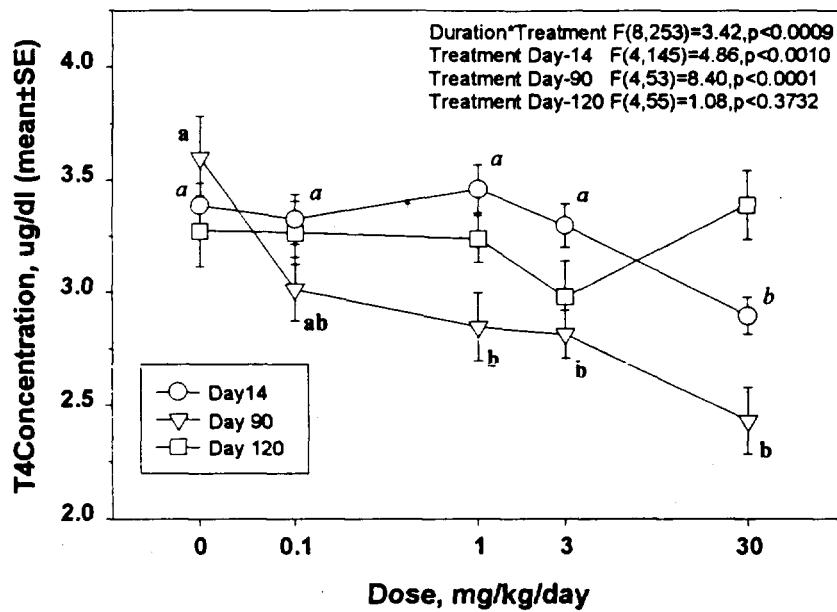


Figure 1. Effects of perchlorate exposure of total serum thyroxine (T4) concentration in a subchronic mouse study. Mice were exposed for 90 days; samples were obtained on Day 14 and 90, and 30 days after cessation of exposure on Day 120. There was a significant interaction of Duration and Treatment, and main effects of Treatment on Days 14 and 90. Means with different letters were significantly different ($p<0.05$). Daily dose was estimated from water consumption data.

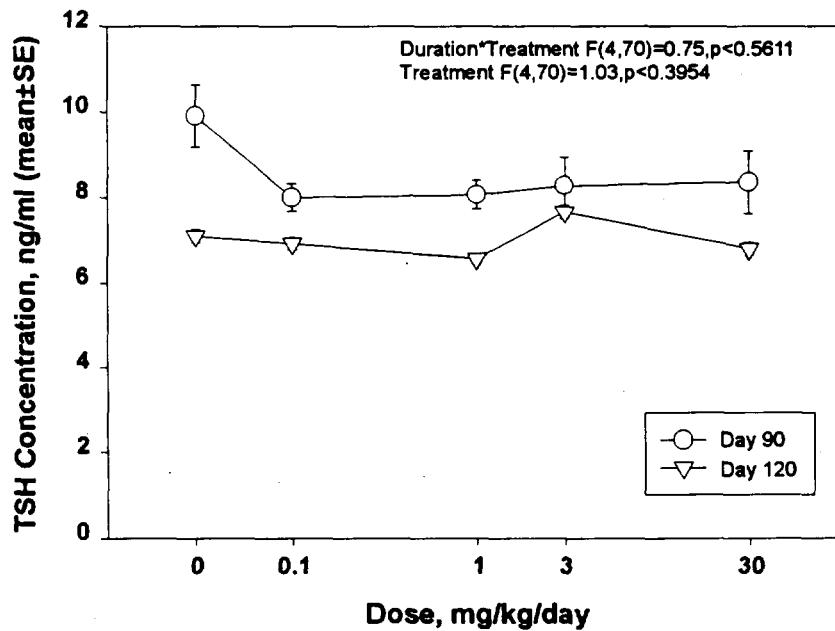


Figure 2. Effects of perchlorate exposure of total serum thyroid stimulation hormone (TSH) concentrations in a subchronic mouse study. Mice were exposed for 90 days; samples were obtained at the end of exposure (Day 90) and 30 days after cessation of exposure on Day 120. There was a no significant interaction of Duration and Treatment, nor was there a main effect of Treatment. Daily dose was estimated from water consumption data.

APPENDIX 1 - Email messages

Mail Envelope Info: (362280E8.C6C : 17 : 35948)

Subject: Re: ps

Creation Date: 10/12/98 6:21pm

From: Deborah Keil <keilde@musc.edu>

Created By: RTPNHEERL01.IN:"keilde@musc.edu"

Recipients

Post Office RTPNHEERL01.NH-ERC1

CROFTON-KEVIN (KEVIN CROFTON)

Domain.Post Office Route

RTPNHEERL01.NH-ERC1 RTPNHEERL01.NH-ERC1

Files Size Date & Time

MESSAGE 902 10/12/98 06:21pm

Header 874

Kevin,

I checked and your spreadsheet matches my most current data tables.

The 90d "D" T4 results that you have in the spreadsheet (one of the red areas) were obtained from a repeated testing (second run).

This was a more efficient run than the earlier reported 90d "D" run and this may be the source of the confusion. Missing values (#14 and 15) in this experiment (90d "D") indicates insufficient sample on the retest.

In addition, the TSH results for the 90d "A" study (the other red area) is also correct.

I will verify all numbers that are one significant digit tomorrow from original data. I anticipate that the second significant digit is a zero that was not formatted into the spreadsheet.

Deborah Keil

Appendix 1 (con't)

Mail Envelope Info: (36237634.E75 : 13 : 36469)

Subject: Re: ps

Creation Date: 10/13/98 11:47am

From: Deborah Keil <keilde@musc.edu>

Created By: RTPNHEERL01.IN:"keilde@musc.edu"

Recipients

Post Office RTPNHEERL01.NH-ERC1

CROFTON-KEVIN (KEVIN CROFTON)

Domain.Post Office Route

RTPNHEERL01.NH-ERC1 RTPNHEERL01.NH-ERC1

Files Size Date & Time

MESSAGE 303 10/13/98 11:47am

th_mouse.xls 48128

Header 915

Kevin,

I confirmed the value for the first decimal place on your spreadsheet and have attached this to the email.

Deborah

KEVIN CROFTON wrote:

> any way you can increase the significant digits in the spreadsheet files? e.g. TSH is reported as
> 7 ng/ml. Surely this is not 7.000 ng/ml.

>

> kevin

11 The SAS System 22:30 Sunday, October 18, 1998

NOTE: Copyright © 1989-1996 by SAS Institute Inc., Cary, NC, USA.
NOTE: SAS (r) Proprietary Software Release 6.12 TS020
Licensed to US ENVIRONMENTAL PROTECTION AGENCY, Site 0019614059.

NOTE: Running on ALPHASERVER Model 2100 5/300 Serial Number 80000000.

Welcome to the NHEERL-RTP SAS Information Delivery System.

```
1      *THIS FILE IS FOUND AT [CROfton.THYROID.perchlorate]perchlorate_mouse_TH.SAS;
2      *IT ANALYZES THE THYROID HORMONE DATA FROM THE MOUSE IMMUNOTOX PERCHLORATE STUDY;
3
4
5      *INPUT DATA INTO SAS DATASET;
6      DATA RAW; INFILE '[CROFTON.THYROID.PERCHLORATE]PERCHLORATE_MOUSE_TH';
7          INPUT DUR DAY$ LETTER$ DURATION STUDY $ TRT $ ANIM $ T4 TSH;
8
```

NOTE: The infile '[CROFTON.THYROID.PERCHLORATE]PERCHLORATE_MOUSE_TH' is:
File=DSA21:[SAS\$USERS.CROFTON.THYROID.PERCHLORATE]PERCHLORATE_MOUSE_TH.DAT
NOTE: 270 records were read from the infile '[CROFTON.THYROID.PERCHLORATE]PERCHLORATE_MOUSE_TH'.
The minimum record length was 81.
The maximum record length was 83.
NOTE: The data set WORK.RAW has 270 observations and 9 variables.

```
9          PROC PRINT;
10
11      *SORT DATA BY TRT -- THEN GET MEANS;
12
```

NOTE: The PROCEDURE PRINT printed pages 1-5.

```
12      PROC SORT; BY TRT;
13
```

NOTE: The data set WORK.RAW has 270 observations and 9 variables.

```
13      PROC MEANS N MEAN STDERR MIN MAX STD VAR CV; BY TRT;
14          VAR T4 TSH;
15
16      *SORT DATA BY DURATION AND TRT -- THEN GET MEANS;
17
```

NOTE: The PROCEDURE MEANS printed page 6.

```
17      PROC SORT; BY DURATION TRT;
18
```

NOTE: The data set WORK.RAW has 270 observations and 9 variables.

```
18      PROC MEANS N MEAN STDERR MIN MAX STD VAR CV; BY DURATION TRT;
19          VAR T4 TSH;
20
21      *SORT DATA BY STUDY, DURATION AND TRT -- THEN GET MEANS;
22
```

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NOTE: The PROCEDURE MEANS printed pages 7-9.

```
22      PROC SORT; BY STUDY DURATION TRT;  
23
```

NOTE: The data set WORK.RAW has 270 observations and 9 variables.

```
23      PROC MEANS N MEAN STDERR MIN MAX STD VAR CV; BY STUDY DURATION TRT;  
24          VAR T4 TSH;  
25  
26  
27      *RUN TWO WAY ANOVAs - DURATION TRT - FOR ALL VARIABLES;  
28
```

NOTE: The PROCEDURE MEANS printed pages 10-17.

```
28      PROC SORT; BY DURATION TRT;  
29
```

NOTE: The data set WORK.RAW has 270 observations and 9 variables.

```
29      PROC GLM;  
30          CLASSES DURATION TRT;  
31          MODEL T4 TSH = DURATION|TRT;  
32          TITLE1 "MOUSE IMMUNOTOX THYROID HORMONE DATA";  
33          TITLE2 "PROC GLM - STUDY BY TRT INTERACTIONS";  
34  
35  
36      *STEPDOWN ANOVAs - DATA COLLAPSED ACROSS STUDY - ANOVAs AT EACH DURATION;
```

NOTE: The PROCEDURE GLM printed pages 18-20.

```
37      PROC SORT; BY DURATION TRT;
```

NOTE: Input data set is already sorted, no sorting done.

```
38      PROC GLM; BY DURATION;  
39          CLASSES TRT;  
40          MODEL T4 TSH = TRT;  
41          MEANS TRT/TUKEY LINE;  
42          TITLE1 "MOUSE IMMUNOTOX THYROID HORMONE DATA";  
43          TITLE2 "PROC GLM - COLLAPSED ACROSS STUDIES";  
44  
45  
46      ENDSAS;
```

NOTE: The PROCEDURE GLM printed pages 21-33.

NOTE: SAS Institute Inc., SAS Campus Drive, Cary, NC USA 27513-2414

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OBS	DUR	DAY	LETTER	DURATION	STUDY	TRT	ANIM	T4	TSH
1	120	d	B	120	B	Control	1B	3.5	6.20
2	120	d	B	120	B	Control	2B	4.1	7.10
3	120	d	B	120	B	Control	3B	3.3	7.10
4	120	d	B	120	B	Control	4B	2.5	8.00
5	120	d	B	120	B	Control	5B	3.0	6.20
6	120	d	B	120	B	Control	6B	2.5	8.00
7	120	d	B	120	B	0.1-mg/k	7B	3.1	8.00
8	120	d	B	120	B	0.1-mg/k	8B	3.1	7.10
9	120	d	B	120	B	0.1-mg/k	9B	3.5	8.00
10	120	d	B	120	B	0.1-mg/k	10B	2.8	8.80
11	120	d	B	120	B	0.1-mg/k	11B	3.5	3.40
12	120	d	B	120	B	0.1-mg/k	12B	3.0	6.20
13	120	d	B	120	B	1.0-mg/k	13B	3.1	6.20
14	120	d	B	120	B	1.0-mg/k	14B	3.3	5.45
15	120	d	B	120	B	1.0-mg/k	15B	3.7	5.45
16	120	d	B	120	B	1.0-mg/k	16B	3.5	10.65
17	120	d	B	120	B	1.0-mg/k	17B	2.8	6.20
18	120	d	B	120	B	1.0-mg/k	18B	3.1	5.45
19	120	d	B	120	B	3.0-mg/k	19B	2.7	7.10
20	120	d	B	120	B	3.0-mg/k	20B	2.5	8.00
21	120	d	B	120	B	3.0-mg/k	21B	2.5	8.80
22	120	d	B	120	B	3.0-mg/k	22B	2.5	3.40
23	120	d	B	120	B	3.0-mg/k	23B	3.3	8.80
24	120	d	B	120	B	3.0-mg/k	24B	2.7	9.80
25	120	d	B	120	B	30.0-mg/	25B	2.7	6.20
26	120	d	B	120	B	30.0-mg/	26B	3.5	7.10
27	120	d	B	120	B	30.0-mg/	27B	3.7	9.80
28	120	d	B	120	B	30.0-mg/	28B	3.1	5.45
29	120	d	B	120	B	30.0-mg/	29B	3.1	3.40
30	120	d	B	120	B	30.0-mg/	30B	3.5	8.80
31	120	d	E	120	E	Control	1	3.7	.
32	120	d	E	120	E	Control	2	3.5	.
33	120	d	E	120	E	Control	3	3.3	.
34	120	d	E	120	E	Control	4	4.1	.
35	120	d	E	120	E	Control	5	2.7	.
36	120	d	E	120	E	Control	6	3.1	.
37	120	d	E	120	E	0.1-mg/k	7	2.4	.
38	120	d	E	120	E	0.1-mg/k	8	2.8	.
39	120	d	E	120	E	0.1-mg/k	9	3.9	.
40	120	d	E	120	E	0.1-mg/k	10	3.5	.
41	120	d	E	120	E	0.1-mg/k	11	4.1	.
42	120	d	E	120	E	0.1-mg/k	12	3.5	.
43	120	d	E	120	E	1.0-mg/k	13	3.7	.
44	120	d	E	120	E	1.0-mg/k	14	2.7	.
45	120	d	E	120	E	1.0-mg/k	15	3.5	.
46	120	d	E	120	E	1.0-mg/k	16	2.7	.
47	120	d	E	120	E	1.0-mg/k	17	3.5	.
48	120	d	E	120	E	1.0-mg/k	18	3.3	.
49	120	d	E	120	E	3.0-mg/k	19	2.8	.
50	120	d	E	120	E	3.0-mg/k	20	3.1	.
51	120	d	E	120	E	3.0-mg/k	21	3.1	.
52	120	d	E	120	E	3.0-mg/k	22	3.0	.
53	120	d	E	120	E	3.0-mg/k	23	4.5	.
54	120	d	E	120	E	3.0-mg/k	24	3.1	.
55	120	d	E	120	E	30.0-mg/	25	3.3	.
56	120	d	E	120	E	30.0-mg/	26	3.1	.

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1

OBS	DUR	DAY	LETTER	DURATION	STUDY	TRT	ANIM	T4	TSH
57	120	d	E	120	E	30.0-mg/	27	3.0	.
58	120	d	E	120	E	30.0-mg/	28	3.1	.
59	120	d	E	120	E	30.0-mg/	29	4.7	.
60	120	d	E	120	E	30.0-mg/	30	3.9	.
61	90	d	A	90	A	Control	1A	3.7	7.10
62	90	d	A	90	A	Control	2A	5.0	12.65
63	90	d	A	90	A	Control	3A	3.7	13.65
64	90	d	A	90	A	Control	4A	3.1	11.65
65	90	d	A	90	A	Control	5A	3.1	8.80
66	90	d	A	90	A	Control	6A	2.7	8.00
67	90	d	A	90	A	0.1-mg/k	7A	2.8	7.10
68	90	d	A	90	A	0.1-mg/k	8A	3.7	8.00
69	90	d	A	90	A	0.1-mg/k	9A	3.3	7.10
70	90	d	A	90	A	0.1-mg/k	10A	2.4	8.00
71	90	d	A	90	A	0.1-mg/k	11A	3.5	8.00
72	90	d	A	90	A	0.1-mg/k	12A	2.7	8.00
73	90	d	A	90	A	1.0-mg/k	13A	3.1	7.10
74	90	d	A	90	A	1.0-mg/k	14A	2.7	8.00
75	90	d	A	90	A	1.0-mg/k	15A	2.8	8.80
76	90	d	A	90	A	1.0-mg/k	16A	3.0	8.80
77	90	d	A	90	A	1.0-mg/k	17A	3.7	7.10
78	90	d	A	90	A	1.0-mg/k	18A	3.3	8.00
79	90	d	A	90	A	3.0-mg/k	19A	3.1	5.45
80	90	d	A	90	A	3.0-mg/k	20A	3.5	5.45
81	90	d	A	90	A	3.0-mg/k	21A	2.8	7.10
82	90	d	A	90	A	3.0-mg/k	22A	2.5	8.00
83	90	d	A	90	A	3.0-mg/k	23A	2.8	7.10
84	90	d	A	90	A	3.0-mg/k	24A	2.8	8.80
85	90	d	A	90	A	30.0-mg/	25A	1.8	5.45
86	90	d	A	90	A	30.0-mg/	26A	2.1	11.65
87	90	d	A	90	A	30.0-mg/	27A	3.7	8.00
88	90	d	A	90	A	30.0-mg/	28A	2.1	8.80
89	90	d	A	90	A	30.0-mg/	29A	2.8	7.10
90	90	d	A	90	A	30.0-mg/	30A	2.8	9.80
91	90	d	D	90	D	Control	1D	3.0	7.10
92	90	d	D	90	D	Control	2D	4.1	10.65
93	90	d	D	90	D	Control	3D	3.3	8.80
94	90	d	D	90	D	Control	4D	4.3	10.65
95	90	d	D	90	D	Control	5D	3.7	.
96	90	d	D	90	D	Control	6D	3.5	.
97	90	d	D	90	D	0.1-mg/k	7D	2.8	8.00
98	90	d	D	90	D	0.1-mg/k	8D	3.0	10.65
99	90	d	D	90	D	0.1-mg/k	9D	3.9	8.00
100	90	d	D	90	D	0.1-mg/k	10D	2.5	7.10
101	90	d	D	90	D	0.1-mg/k	11D	2.5	.
102	90	d	D	90	D	0.1-mg/k	12D	3.1	.
103	90	d	D	90	D	1.0-mg/k	13D	2.4	8.00
104	90	d	D	90	D	1.0-mg/k	14D	.	.
105	90	d	D	90	D	1.0-mg/k	15D	.	.
106	90	d	D	90	D	1.0-mg/k	16D	2.1	9.80
107	90	d	D	90	D	1.0-mg/k	17D	3.0	8.80
108	90	d	D	90	D	1.0-mg/k	18D	2.4	6.20
109	90	d	D	90	D	3.0-mg/k	19D	2.7	8.80
110	90	d	D	90	D	3.0-mg/k	20D	3.3	9.80
111	90	d	D	90	D	3.0-mg/k	21D	2.5	12.65
112	90	d	D	90	D	3.0-mg/k	22D	2.4	7.10

OBS	DUR	DAY	LETTER	DURATION	STUDY	TRT	ANIM	T4	TSH
OBS	DUR	DAY	LETTER	DURATION	STUDY	TRT	ANIM	T4	TSH
OBS	DUR	DAY	LETTER	DURATION	STUDY	TRT	ANIM	T4	TSH
113	90	d	D	90	D	3.0-mg/k	23D	2.30	10.65
114	90	d	D	90	D	3.0-mg/k	24D	3.10	9.80
115	90	d	D	90	D	3.0-mg/k	25D	2.10	6.20
116	90	d	D	90	D	3.0-mg/k	26D	2.50	22.60
117	90	d	D	90	D	3.0-mg/k	27D	2.40	.
118	90	d	D	90	D	3.0-mg/k	28D	2.50	.
119	90	d	D	90	D	3.0-mg/k	29D	1.90	.
120	90	d	D	90	D	30.0-mg/	30D	2.50	.
121	14	d	C	14	C	Control	1C	3.30	.
122	14	d	C	14	C	Control	2C	4.30	.
123	14	d	C	14	C	Control	3C	3.70	.
124	14	d	C	14	C	Control	4C	3.80	.
125	14	d	C	14	C	Control	5C	2.80	.
126	14	d	C	14	C	Control	6C	3.00	.
127	14	d	C	14	C	0.1-mg/k	7C	2.50	.
128	14	d	C	14	C	0.1-mg/k	8C	3.20	.
129	14	d	C	14	C	0.1-mg/k	9C	2.20	.
130	14	d	C	14	C	0.1-mg/k	10C	3.20	.
131	14	d	C	14	C	0.1-mg/k	11C	3.30	.
132	14	d	C	14	C	0.1-mg/k	12C	3.50	.
133	14	d	C	14	C	1.0-mg/k	13C	2.10	.
134	14	d	C	14	C	1.0-mg/k	14C	3.00	.
135	14	d	C	14	C	1.0-mg/k	15C	3.00	.
136	14	d	C	14	C	1.0-mg/k	16C	3.20	.
137	14	d	C	14	C	1.0-mg/k	17C	2.80	.
138	14	d	C	14	C	1.0-mg/k	18C	2.50	.
139	14	d	C	14	C	3.0-mg/k	19C	2.40	.
140	14	d	C	14	C	3.0-mg/k	20C	2.80	.
141	14	d	C	14	C	3.0-mg/k	21C	2.80	.
142	14	d	C	14	C	3.0-mg/k	22C	3.20	.
143	14	d	C	14	C	3.0-mg/k	23C	2.20	.
144	14	d	C	14	C	3.0-mg/k	24C	2.40	.
145	14	d	C	14	C	3.0-mg/k	25C	2.70	.
146	14	d	C	14	C	3.0-mg/k	26C	2.00	.
147	14	d	C	14	C	3.0-mg/k	27C	2.50	.
148	14	d	C	14	C	3.0-mg/k	28C	3.00	.
149	14	d	C	14	C	3.0-mg/k	29C	2.80	.
150	14	d	C	14	C	30.0-mg/	30C	3.30	.
151	14	d	I	14	I	Control	1I	3.40	.
152	14	d	I	14	I	Control	2I	3.40	.
153	14	d	I	14	I	Control	3I	3.10	.
154	14	d	I	14	I	Control	4I	3.25	.
155	14	d	I	14	I	Control	5I	3.95	.
156	14	d	I	14	I	Control	6I	2.75	.
157	14	d	I	14	I	0.1-mg/k	7I	3.55	.
158	14	d	I	14	I	0.1-mg/k	8I	3.40	.
159	14	d	I	14	I	0.1-mg/k	9I	3.95	.
160	14	d	I	14	I	0.1-mg/k	10I	3.55	.
161	14	d	I	14	I	0.1-mg/k	11I	2.95	.
162	14	d	I	14	I	0.1-mg/k	12I	3.40	.
163	14	d	I	14	I	0.1-mg/k	13I	3.40	.
164	14	d	I	14	I	0.1-mg/k	14I	3.10	.
165	14	d	I	14	I	1.0-mg/k	15I	3.25	.
166	14	d	I	14	I	1.0-mg/k	16I	3.70	.
167	14	d	I	14	I	1.0-mg/k	17I	3.40	.
168	14	d	I	14	I	1.0-mg/k	18I	3.25	.

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169	14	d	I	14	I	3.0-mg/k	19I	2.75	.
170	14	d	I	14	I	3.0-mg/k	20I	3.40	.
171	14	d	I	14	I	3.0-mg/k	21I	2.95	.
172	14	d	I	14	I	3.0-mg/k	22I	3.40	.
173	14	d	I	14	I	3.0-mg/k	23I	2.95	.
174	14	d	I	14	I	3.0-mg/k	24I	3.10	.
175	14	d	I	14	I	30.0-mg/	25I	3.40	.
176	14	d	I	14	I	30.0-mg/	26I	2.60	.
177	14	d	I	14	I	30.0-mg/	27I	2.15	.
178	14	d	I	14	I	30.0-mg/	28I	2.15	.
179	14	d	I	14	I	30.0-mg/	29I	3.10	.
180	14	d	I	14	I	30.0-mg/	30I	2.95	.
181	14	d	J	14	J	Control	1J	2.75	.
182	14	d	J	14	J	Control	2J	3.90	.
183	14	d	J	14	J	Control	3J	2.95	.
184	14	d	J	14	J	Control	4J	3.40	.
185	14	d	J	14	J	Control	5J	3.90	.
186	14	d	J	14	J	Control	6J	3.90	.
187	14	d	J	14	J	0.1-mg/k	7J	3.90	.
188	14	d	J	14	J	0.1-mg/k	8J	2.95	.
189	14	d	J	14	J	0.1-mg/k	9J	3.40	.
190	14	d	J	14	J	0.1-mg/k	10J	3.40	.
191	14	d	J	14	J	0.1-mg/k	11J	3.70	.
192	14	d	J	14	J	0.1-mg/k	12J	3.40	.
193	14	d	J	14	J	1.0-mg/k	13J	2.95	.
194	14	d	J	14	J	1.0-mg/k	14J	3.70	.
195	14	d	J	14	J	1.0-mg/k	15J	3.10	.
196	14	d	J	14	J	1.0-mg/k	16J	3.90	.
197	14	d	J	14	J	1.0-mg/k	17J	3.10	.
198	14	d	J	14	J	1.0-mg/k	18J	3.55	.
199	14	d	J	14	J	3.0-mg/k	19J	3.25	.
200	14	d	J	14	J	3.0-mg/k	20J	3.55	.
201	14	d	J	14	J	3.0-mg/k	21J	3.25	.
202	14	d	J	14	J	3.0-mg/k	22J	3.70	.
203	14	d	J	14	J	3.0-mg/k	23J	3.90	.
204	14	d	J	14	J	3.0-mg/k	24J	3.40	.
205	14	d	J	14	J	30.0-mg/	25J	3.25	.
206	14	d	J	14	J	30.0-mg/	26J	3.25	.
207	14	d	J	14	J	30.0-mg/	27J	3.40	.
208	14	d	J	14	J	30.0-mg/	28J	2.95	.
209	14	d	J	14	J	30.0-mg/	29J	2.95	.
210	14	d	J	14	J	30.0-mg/	30J	3.25	.
211	14	d	G	14	G	Control	1G	2.70	.
212	14	d	G	14	G	Control	2G	3.00	.
213	14	d	G	14	G	Control	3G	2.80	.
214	14	d	G	14	G	Control	4G	3.00	.
215	14	d	G	14	G	Control	5G	3.50	.
216	14	d	G	14	G	Control	6G	2.40	.
217	14	d	G	14	G	0.1-mg/k	7G	2.20	.
218	14	d	G	14	G	0.1-mg/k	8G	2.70	.
219	14	d	G	14	G	0.1-mg/k	9G	3.00	.
220	14	d	G	14	G	0.1-mg/k	10G	3.60	.
221	14	d	G	14	G	0.1-mg/k	11G	2.80	.
222	14	d	G	14	G	0.1-mg/k	12G	2.40	.
223	14	d	G	14	G	1.0-mg/k	13G	3.30	.
224	14	d	G	14	G	1.0-mg/k	14G	3.00	.

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OBS	DUR	DAY	LETTER	DURATION	STUDY	TRT	ANIM	T4	TSH
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225	14	d	G	14	G	1.0-mg/k	15G	4.1	.
226	14	d	G	14	G	1.0-mg/k	16G	3.7	.
227	14	d	G	14	G	1.0-mg/k	17G	3.5	.
228	14	d	G	14	G	1.0-mg/k	18G	3.9	.
229	14	d	G	14	G	3.0-mg/k	19G	3.3	.
230	14	d	G	14	G	3.0-mg/k	20G	3.3	.
231	14	d	G	14	G	3.0-mg/k	21G	3.0	.
232	14	d	G	14	G	3.0-mg/k	22G	3.9	.
233	14	d	G	14	G	3.0-mg/k	23G	3.5	.
234	14	d	G	14	G	3.0-mg/k	24G	3.0	.
235	14	d	G	14	G	30.0-mg/	25G	2.8	.
236	14	d	G	14	G	30.0-mg/	26G	3.3	.
237	14	d	G	14	G	30.0-mg/	27G	3.3	.
238	14	d	G	14	G	30.0-mg/	28G	2.0	.
239	14	d	G	14	G	30.0-mg/	29G	2.8	.
240	14	d	G	14	G	30.0-mg/	30G	2.5	.
241	14	d	KK	14	K	Control	1K	3.7	.
242	14	d	KK	14	K	Control	2K	4.8	.
243	14	d	KK	14	K	Control	3K	4.1	.
244	14	d	KK	14	K	Control	4K	3.5	.
245	14	d	KK	14	K	Control	5K	3.5	.
246	14	d	KK	14	K	Control	6K	3.1	.
247	14	d	KK	14	K	0.1-mg/k	7K	3.1	.
248	14	d	KK	14	K	0.1-mg/k	8K	4.8	.
249	14	d	KK	14	K	0.1-mg/k	9K	3.5	.
250	14	d	KK	14	K	0.1-mg/k	10K	3.7	.
251	14	d	KK	14	K	0.1-mg/k	11K	4.5	.
252	14	d	KK	14	K	0.1-mg/k	12K	4.1	.
253	14	d	KK	14	K	1.0-mg/k	13K	4.5	.
254	14	d	KK	14	K	1.0-mg/k	14K	4.1	.
255	14	d	KK	14	K	1.0-mg/k	15K	4.5	.
256	14	d	KK	14	K	1.0-mg/k	16K	4.5	.
257	14	d	KK	14	K	1.0-mg/k	17K	4.3	.
258	14	d	KK	14	K	1.0-mg/k	18K	3.5	.
259	14	d	KK	14	K	3.0-mg/k	19K	4.1	.
260	14	d	KK	14	K	3.0-mg/k	20K	4.1	.
261	14	d	KK	14	K	3.0-mg/k	21K	4.1	.
262	14	d	KK	14	K	3.0-mg/k	22K	4.3	.
263	14	d	KK	14	K	3.0-mg/k	23K	3.5	.
264	14	d	KK	14	K	3.0-mg/k	24K	3.5	.
265	14	d	KK	14	K	30.0-mg/	25K	2.5	.
266	14	d	KK	14	K	30.0-mg/	26K	2.9	.
267	14	d	KK	14	K	30.0-mg/	27K	3.3	.
268	14	d	KK	14	K	30.0-mg/	28K	3.1	.
269	14	d	KK	14	K	30.0-mg/	29K	3.1	.
270	14	d	K	14	K	30.0-mg/	30K	3.7	.

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----- TRT=0.1-mg/k -----

Variable	N	Mean	Std Error	Minimum	Maximum	Std Dev	Variance	CV
T4	54	3.2453704	0.0765507	2.2000000	4.8000000	0.5625304	0.3164404	17.3333184
TSH	16	7.5906250	0.3686750	3.4000000	10.6500000	1.4746998	2.1747396	19.4279105

----- TRT=1.0-mg/k -----

Variable	N	Mean	Std Error	Minimum	Maximum	Std Dev	Variance	CV
T4	52	3.2942308	0.0785384	2.1000000	4.5000000	0.5663483	0.3207504	17.1921253
TSH	16	7.5000000	0.4032679	5.4500000	10.6500000	1.6130716	2.6020000	21.5076214

----- TRT=3.0-mg/k -----

Variable	N	Mean	Std Error	Minimum	Maximum	Std Dev	Variance	CV
T4	54	3.1222222	0.0730640	2.2000000	4.5000000	0.5369082	0.2882704	17.1963488
TSH	17	8.0470588	0.5252883	3.4000000	12.6500000	2.1658190	4.6907721	26.9144177

----- TRT=30.0-mg/ -----

Variable	N	Mean	Std Error	Minimum	Maximum	Std Dev	Variance	CV
T4	54	2.9055556	0.0774288	1.8000000	4.7000000	0.5689834	0.3237421	19.5826036
TSH	15	8.6766667	1.1399234	3.4000000	22.6000000	4.4149044	19.4913810	50.8824942

----- TRT=Control -----

Variable	N	Mean	Std Error	Minimum	Maximum	Std Dev	Variance	CV
T4	54	3.4101852	0.0772449	2.4000000	5.0000000	0.5676316	0.3222056	16.6451838
TSH	16	8.8531250	0.5783142	6.2000000	13.6500000	2.3132566	5.3511563	26.1292666

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----- DURATION=14 TRT=0.1-mg/k -----

Variable	N	Mean	Std Error	Minimum	Maximum	Std Dev	Variance	CV
T4	30	3.3283333	0.1105286	2.2000000	4.8000000	0.6053901	0.3664971	18.1889853
TSH	0

----- DURATION=14 TRT=1.0-mg/k -----

Variable	N	Mean	Std Error	Minimum	Maximum	Std Dev	Variance	CV
T4	30	3.4633333	0.1073166	2.1000000	4.5000000	0.5877974	0.3455057	16.9720126
TSH	0

----- DURATION=14 TRT=3.0-mg/k -----

Variable	N	Mean	Std Error	Minimum	Maximum	Std Dev	Variance	CV
T4	30	3.3000000	0.0966389	2.2000000	4.3000000	0.5293132	0.2801724	16.0397925
TSH	0

----- DURATION=14 TRT=30.0-mg/ -----

Variable	N	Mean	Std Error	Minimum	Maximum	Std Dev	Variance	CV
T4	30	2.9000000	0.0807294	2.0000000	3.7000000	0.4421733	0.1955172	15.2473557
TSH	0

----- DURATION=14 TRT=Control -----

Variable	N	Mean	Std Error	Minimum	Maximum	Std Dev	Variance	CV
T4	30	3.3883333	0.0995878	2.4000000	4.8000000	0.5454646	0.2975316	16.0983152
TSH	0

----- DURATION=90 TRT=0.1-mg/k -----

Variable	N	Mean	Std Error	Minimum	Maximum	Std Dev	Variance	CV
T4	12	3.0166667	0.1424001	2.4000000	3.9000000	0.4932883	0.2433333	16.3520979
TSH	10	7.9950000	0.3240756	7.1000000	10.6500000	1.0248171	1.0502500	12.8182246

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----- DURATION=90 TRT=1.0-mg/k -----

Variable	N	Mean	Std Error	Minimum	Maximum	Std Dev	Variance	CV
T4	10	2.8500000	0.1500000	2.1000000	3.7000000	0.4743416	0.2250000	16.6435666
TSH	10	8.0600000	0.3330666	6.2000000	9.8000000	1.0532489	1.1093333	13.0676047

----- DURATION=90 TRT=3.0-mg/k -----

Variable	N	Mean	Std Error	Minimum	Maximum	Std Dev	Variance	CV
T4	12	2.8166667	0.1071909	2.3000000	3.5000000	0.3713203	0.1378788	13.1829703
TSH	11	8.2636364	0.6594450	5.4500000	12.6500000	2.1871318	4.7835455	26.4669413

----- DURATION=90 TRT=30.0-mg/ -----

Variable	N	Mean	Std Error	Minimum	Maximum	Std Dev	Variance	CV
T4	12	2.4333333	0.1483921	1.8000000	3.7000000	0.5140452	0.2642424	21.1251435
TSH	9	9.9333333	1.7099180	5.4500000	22.6000000	5.1297539	26.3143750	51.6418177

----- DURATION=90 TRT=Control -----

Variable	N	Mean	Std Error	Minimum	Maximum	Std Dev	Variance	CV
T4	12	3.6000000	0.1846372	2.7000000	5.0000000	0.6396021	0.4090909	17.7667264
TSH	10	9.9050000	0.7266533	7.1000000	13.6500000	2.2978795	5.2802500	23.1991868

----- DURATION=120 TRT=0.1-mg/k -----

Variable	N	Mean	Std Error	Minimum	Maximum	Std Dev	Variance	CV
T4	12	3.2666667	0.1410638	2.4000000	4.1000000	0.4886593	0.2387879	14.9589571
TSH	6	6.9166667	0.7917982	3.4000000	8.8000000	1.9395017	3.7616667	28.0409878

----- DURATION=120 TRT=1.0-mg/k -----

Variable	N	Mean	Std Error	Minimum	Maximum	Std Dev	Variance	CV
T4	12	3.2416667	0.1047785	2.7000000	3.7000000	0.3629634	0.1317424	11.1968142
TSH	6	6.5666667	0.8303279	5.4500000	10.6500000	2.0338797	4.1366667	30.9727874

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----- DURATION=120 TRT=3.0-mg/k -----

Variable	N	Mean	Std Error	Minimum	Maximum	Std Dev	Variance	CV
T4	12	2.9833333	0.1589899	2.5000000	4.5000000	0.5507571	0.3033333	18.4611303
TSH	6	7.6500000	0.9265528	3.4000000	9.8000000	2.2695815	5.1510000	29.6677315

----- DURATION=120 TRT=30.0-mg/ -----

Variable	N	Mean	Std Error	Minimum	Maximum	Std Dev	Variance	CV
T4	12	3.3916667	0.1524836	2.7000000	4.7000000	0.5282188	0.2790152	15.5740201
TSH	6	6.7916667	0.9457287	3.4000000	9.8000000	2.3165528	5.3664167	34.1087522

----- DURATION=120 TRT=Control -----

Variable	N	Mean	Std Error	Minimum	Maximum	Std Dev	Variance	CV
T4	12	3.2750000	0.1576941	2.5000000	4.1000000	0.5462683	0.2984091	16.6799491
TSH	6	7.1000000	0.3286335	6.2000000	8.0000000	0.8049845	0.6480000	11.3378095

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--- STUDY=A DURATION=90 TRT=0.1-mg/k ---

Variable	N	Mean	Std Error	Minimum	Maximum	Std Dev	Variance	CV
T4	6	3.0666667	0.2076322	2.4000000	3.7000000	0.5085928	0.2586667	16.5845488
TSH	6	7.000000	0.1897367	7.1000000	8.0000000	0.4647580	0.2160000	6.0358182

--- STUDY=A DURATION=90 TRT=1.0-mg/k ---

Variable	N	Mean	Std Error	Minimum	Maximum	Std Dev	Variance	CV
T4	6	3.1000000	0.1483240	2.7000000	3.7000000	0.3633180	0.1320000	11.7199369
TSH	6	7.9666667	0.3105551	7.1000000	8.8000000	0.7607014	0.5786667	9.5485535

--- STUDY=A DURATION=90 TRT=3.0-mg/k ---

Variable	N	Mean	Std Error	Minimum	Maximum	Std Dev	Variance	CV
T4	6	2.9166667	0.1400397	2.5000000	3.5000000	0.3430258	0.1176667	11.7608829
TSH	6	6.9833333	0.5496464	5.4500000	8.8000000	1.3463531	1.8126667	19.2795193

--- STUDY=A DURATION=90 TRT=30.0-mg/ ---

Variable	N	Mean	Std Error	Minimum	Maximum	Std Dev	Variance	CV
T4	6	2.5500000	0.2837252	1.8000000	3.7000000	0.6949820	0.4830000	27.2541966
TSH	6	8.4666667	0.8795517	5.4500000	11.6500000	2.1544528	4.6416667	25.4462924

--- STUDY=A DURATION=90 TRT=Control ---

Variable	N	Mean	Std Error	Minimum	Maximum	Std Dev	Variance	CV
T4	6	3.5500000	0.3304038	2.7000000	5.0000000	0.8093207	0.6550000	22.7977663
TSH	6	10.3083333	1.1007132	7.1000000	13.6500000	2.6961856	7.2694167	26.1553977

--- STUDY=B DURATION=120 TRT=0.1-mg/k ---

Variable	N	Mean	Std Error	Minimum	Maximum	Std Dev	Variance	CV
T4	6	3.1666667	0.1145038	2.8000000	3.5000000	0.2804758	0.0786667	8.8571301
TSH	6	6.9166667	0.7917982	3.4000000	8.8000000	1.9395017	3.7616667	28.0409878

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----- STUDY=B DURATION=120 TRT=1.0-mg/k -----

Variable	N	Mean	Std Error	Minimum	Maximum	Std Dev	Variance	CV
T4	6	3.2500000	0.1310216	2.8000000	3.7000000	0.3209361	0.1030000	9.8749579
TSH	6	6.666667	0.8303279	5.4500000	10.6500000	2.0338797	4.1366667	30.9727874

----- STUDY=B DURATION=120 TRT=3.0-mg/k -----

Variable	N	Mean	Std Error	Minimum	Maximum	Std Dev	Variance	CV
T4	6	2.7000000	0.1264911	2.5000000	3.3000000	0.3098387	0.0960000	11.4755062
TSH	6	7.6500000	0.9265528	3.4000000	9.8000000	2.2695815	5.1510000	29.6677315

----- STUDY=B DURATION=120 TRT=30.0-mg/k -----

Variable	N	Mean	Std Error	Minimum	Maximum	Std Dev	Variance	CV
T4	6	3.2666667	0.1498147	2.7000000	3.7000000	0.3669696	0.1346667	11.2337624
TSH	6	6.7916667	0.9457287	3.4000000	9.8000000	2.3165528	5.3664167	34.1087522

----- STUDY=B DURATION=120 TRT=Control -----

Variable	N	Mean	Std Error	Minimum	Maximum	Std Dev	Variance	CV
T4	6	3.1500000	0.2526526	2.5000000	4.1000000	0.6188699	0.3830000	19.6466647
TSH	6	7.1000000	0.3286335	6.2000000	8.0000000	0.8049845	0.6480000	11.3378095

----- STUDY=C DURATION=14 TRT=0.1-mg/k -----

Variable	N	Mean	Std Error	Minimum	Maximum	Std Dev	Variance	CV
T4	6	2.9833333	0.2088327	2.2000000	3.5000000	0.5115336	0.2616667	17.1463791
TSH	0

----- STUDY=C DURATION=14 TRT=1.0-mg/k -----

Variable	N	Mean	Std Error	Minimum	Maximum	Std Dev	Variance	CV
T4	6	2.7666667	0.1646545	2.1000000	3.2000000	0.4033196	0.1626667	14.5778154
TSH	0

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----- STUDY=C DURATION=14 TRT=3.0-mg/k -----

Variable	N	Mean	Std Error	Minimum	Maximum	Std Dev	Variance	CV
T4	6	2.6333333	0.1498147	2.2000000	3.2000000	0.3669696	0.1346667	13.9355534
TSH	0

----- STUDY=C DURATION=14 TRT=30.0-mg/ -----

Variable	N	Mean	Std Error	Minimum	Maximum	Std Dev	Variance	CV
T4	6	2.7166667	0.1815060	2.0000000	3.3000000	0.4445972	0.1976667	16.3655410
TSH	0

----- STUDY=C DURATION=14 TRT=Control -----

Variable	N	Mean	Std Error	Minimum	Maximum	Std Dev	Variance	CV
T4	6	3.4833333	0.2271808	2.8000000	4.3000000	0.5564770	0.3096667	15.9754167
TSH	0

----- STUDY=D DURATION=90 TRT=0.1-mg/k -----

Variable	N	Mean	Std Error	Minimum	Maximum	Std Dev	Variance	CV
T4	6	2.9666667	0.2123938	2.5000000	3.9000000	0.5202563	0.2706667	17.5367308
TSH	4	8.4375000	0.7674023	7.1000000	10.6500000	1.5348045	2.3556250	18.1902761

----- STUDY=D DURATION=90 TRT=1.0-mg/k -----

Variable	N	Mean	Std Error	Minimum	Maximum	Std Dev	Variance	CV
T4	4	2.4750000	0.1887459	2.1000000	3.0000000	0.3774917	0.1425000	15.2521908
TSH	4	8.2000000	0.7615773	6.2000000	9.8000000	1.5231546	2.3200000	18.5750564

----- STUDY=D DURATION=90 TRT=3.0-mg/k -----

Variable	N	Mean	Std Error	Minimum	Maximum	Std Dev	Variance	CV
T4	6	2.7166667	0.1641476	2.3000000	3.3000000	0.4020779	0.1616667	14.8004148
TSH	5	9.8000000	0.9256079	7.1000000	12.6500000	2.0697222	4.2837500	21.1196143

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----- STUDY=D DURATION=90 TRT=30.0-mg/ -----

Variable	N	Mean	Std Error	Minimum	Maximum	Std Dev	Variance	CV
T4	6	2.31666667	0.1046157	1.9000000	2.5000000	0.2562551	0.0656667	11.0613704
TSH	3	12.86666667	4.9763887	6.2000000	22.6000000	8.6193581	74.2933333	66.9898295

----- STUDY=D DURATION=90 TRT=Control -----

Variable	N	Mean	Std Error	Minimum	Maximum	Std Dev	Variance	CV
T4	6	3.6500000	0.1995829	3.0000000	4.3000000	0.4888763	0.2390000	13.3938702
TSH	4	9.3000000	0.8531803	7.1000000	10.6500000	1.7063606	2.9116667	18.3479640

----- STUDY=E DURATION=120 TRT=0.1-mg/k -----

Variable	N	Mean	Std Error	Minimum	Maximum	Std Dev	Variance	CV
T4	6	3.36666667	0.2654137	2.4000000	4.1000000	0.6501282	0.4226667	19.3107384
TSH	0

----- STUDY=E DURATION=120 TRT=1.0-mg/k -----

Variable	N	Mean	Std Error	Minimum	Maximum	Std Dev	Variance	CV
T4	6	3.2333333	0.1763834	2.7000000	3.7000000	0.4320494	0.1866667	13.3623520
TSH	0

----- STUDY=E DURATION=120 TRT=3.0-mg/k -----

Variable	N	Mean	Std Error	Minimum	Maximum	Std Dev	Variance	CV
T4	6	3.26666667	0.2512192	2.8000000	4.5000000	0.6153590	0.3786667	18.8375196
TSH	0

----- STUDY=E DURATION=120 TRT=30.0-mg/ -----

Variable	N	Mean	Std Error	Minimum	Maximum	Std Dev	Variance	CV
T4	6	3.51666667	0.2713137	3.0000000	4.7000000	0.6645801	0.4416667	18.8980114
TSH	0

1

The SAS System

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----- STUDY=E DURATION=120 TRT=Control -----

Variable	N	Mean	Std Error	Minimum	Maximum	Std Dev	Variance	CV
T4	6	3.4000000	0.1983263	2.7000000	4.1000000	0.4857983	0.2360000	14.2881856
TSH	0

----- STUDY=G DURATION=14 TRT=0.1-mg/k -----

Variable	N	Mean	Std Error	Minimum	Maximum	Std Dev	Variance	CV
T4	6	2.7833333	0.2006932	2.2000000	3.6000000	0.4915960	0.2416667	17.6621332
TSH	0

----- STUDY=G DURATION=14 TRT=1.0-mg/k -----

Variable	N	Mean	Std Error	Minimum	Maximum	Std Dev	Variance	CV
T4	6	3.5833333	0.1641476	3.0000000	4.1000000	0.4020779	0.1616667	11.2207796
TSH	0

----- STUDY=G DURATION=14 TRT=3.0-mg/k -----

Variable	N	Mean	Std Error	Minimum	Maximum	Std Dev	Variance	CV
T4	6	3.3333333	0.1382429	3.0000000	3.9000000	0.3386247	0.1146667	10.1587401
TSH	0

----- STUDY=G DURATION=14 TRT=30.0-mg/ -----

Variable	N	Mean	Std Error	Minimum	Maximum	Std Dev	Variance	CV
T4	6	2.7833333	0.2023473	2.0000000	3.3000000	0.4956477	0.2456667	17.8077027
TSH	0

----- STUDY=G DURATION=14 TRT=Control -----

Variable	N	Mean	Std Error	Minimum	Maximum	Std Dev	Variance	CV
T4	6	2.9000000	0.1505545	2.4000000	3.5000000	0.3687818	0.1360000	12.7166130
TSH	0

1

The SAS System

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----- STUDY=I DURATION=14 TRT=0.1-mg/k -----

Variable	N	Mean	Std Error	Minimum	Maximum	Std Dev	Variance	CV
T4	6	3.4666667	0.1320774	2.9500000	3.9500000	0.3235223	0.1046667	9.3323735
TSH	0

----- STUDY=I DURATION=14 TRT=1.0-mg/k -----

Variable	N	Mean	Std Error	Minimum	Maximum	Std Dev	Variance	CV
T4	6	3.3500000	0.0836660	3.1000000	3.7000000	0.2049390	0.0420000	6.1175825
TSH	0

----- STUDY=I DURATION=14 TRT=3.0-mg/k -----

Variable	N	Mean	Std Error	Minimum	Maximum	Std Dev	Variance	CV
T4	6	3.0916667	0.1075614	2.7500000	3.4000000	0.2634704	0.0694167	8.5219546
TSH	0

----- STUDY=I DURATION=14 TRT=30.0-mg/ -----

Variable	N	Mean	Std Error	Minimum	Maximum	Std Dev	Variance	CV
T4	6	2.7250000	0.2100595	2.1500000	3.4000000	0.5145386	0.2647500	18.8821515
TSH	0

----- STUDY=I DURATION=14 TRT=Control -----

Variable	N	Mean	Std Error	Minimum	Maximum	Std Dev	Variance	CV
T4	6	3.3083333	0.1619756	2.7500000	3.9500000	0.3967577	0.1574167	11.9926758
TSH	0

----- STUDY=J DURATION=14 TRT=0.1-mg/k -----

Variable	N	Mean	Std Error	Minimum	Maximum	Std Dev	Variance	CV
T4	6	3.4583333	0.1319196	2.9500000	3.9000000	0.3231357	0.1044167	9.3436823
TSH	0

1

The SAS System

22:30 Sunday, October 18, 1998 16

----- STUDY=J DURATION=14 TRT=1.0-mg/k -----

Variable	N	Mean	Std Error	Minimum	Maximum	Std Dev	Variance	CV
T4	6	3.3833333	0.1574096	2.9500000	3.9000000	0.3855732	0.1486667	11.3962512
TSH	0

----- STUDY=J DURATION=14 TRT=3.0-mg/k -----

Variable	N	Mean	Std Error	Minimum	Maximum	Std Dev	Variance	CV
T4	6	3.5083333	0.1060005	3.2500000	3.9000000	0.2596472	0.0674167	7.4008702
TSH	0

----- STUDY=J DURATION=14 TRT=30.0-mg/ -----

Variable	N	Mean	Std Error	Minimum	Maximum	Std Dev	Variance	CV
T4	6	3.1750000	0.0750000	2.9500000	3.4000000	0.1837117	0.0337500	5.7861962
TSH	0

----- STUDY=J DURATION=14 TRT=Control -----

Variable	N	Mean	Std Error	Minimum	Maximum	Std Dev	Variance	CV
T4	6	3.4666667	0.2120010	2.7500000	3.9000000	0.5192944	0.2696667	14.9796460
TSH	0

----- STUDY=K DURATION=14 TRT=0.1-mg/k -----

Variable	N	Mean	Std Error	Minimum	Maximum	Std Dev	Variance	CV
T4	6	3.9500000	0.2604483	3.1000000	4.8000000	0.6379655	0.4070000	16.1510257
TSH	0

----- STUDY=K DURATION=14 TRT=1.0-mg/k -----

Variable	N	Mean	Std Error	Minimum	Maximum	Std Dev	Variance	CV
T4	6	4.2333333	0.1605546	3.5000000	4.5000000	0.3932768	0.1546667	9.2900039
TSH	0

1

The SAS System

22:30 Sunday, October 18, 1998 17

----- STUDY=K DURATION=14 TRT=3.0-mg/k -----

Variable	N	Mean	Std Error	Minimum	Maximum	Std Dev	Variance	CV
T4	6	3.9333333	0.1406335	3.5000000	4.3000000	0.3444803	0.1186667	8.7579733
TSH	0

----- STUDY=K DURATION=14 TRT=30.0-mg/ -----

Variable	N	Mean	Std Error	Minimum	Maximum	Std Dev	Variance	CV
T4	6	3.1000000	0.1632993	2.5000000	3.7000000	0.4000000	0.1600000	12.9032258
TSH	0

----- STUDY=K DURATION=14 TRT=Control -----

Variable	N	Mean	Std Error	Minimum	Maximum	Std Dev	Variance	CV
T4	6	3.7833333	0.2427848	3.1000000	4.8000000	0.5946988	0.3536667	15.7189111
TSH	0

1

MOUSE IMMUNOTOX THYROID HORMONE DATA 22:30 Sunday, October 18, 1998 18
PROC GLM - STUDY BY TRT INTERACTIONS

General Linear Models Procedure
Class Level Information

Class	Levels	Values
DURATION	3	14 90 120
TRT	5	0.1-mg/k 1.0-mg/k 3.0-mg/k 30.0-mg/ Control

Number of observations in data set = 270

Group	Obs	Dependent Variables
1	268	T4
2	80	TSH

NOTE: Variables in each group are consistent with respect to the presence or absence of missing values.

1

MOUSE IMMUNOTOX THYROID HORMONE DATA 22:30 Sunday, October 18, 1998 19
 PROC GLM - STUDY BY TRT INTERACTIONS

General Linear Models Procedure

Dependent Variable: T4

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	14	20.14201990	1.43871571	5.17	0.0001
Error	253	70.46066667	0.27850066		
Corrected Total	267	90.60268657			
		R-Square	C.V.	Root MSE	T4 Mean
		0.222312	16.51858	0.52773162	3.19477612
Source	DF	Type I SS	Mean Square	F Value	Pr > F
DURATION	2	4.64494289	2.32247144	8.34	0.0003
TRT	4	7.86570597	1.96642649	7.06	0.0001
DURATION*TRT	8	7.63137104	0.95392138	3.43	0.0009
Source	DF	Type III SS	Mean Square	F Value	Pr > F
DURATION	2	4.71871609	2.35935805	8.47	0.0003
TRT	4	6.72973611	1.68243403	6.04	0.0001
DURATION*TRT	8	7.63137104	0.95392138	3.43	0.0009

1 MOUSE IMMUNOTOX THYROID HORMONE DATA 22:30 Sunday, October 18, 1998 20
 PROC GLM - STUDY BY TRT INTERACTIONS

General Linear Models Procedure

Dependent Variable: TSH

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	9	103.19226420	11.46580713	1.91	0.0648
Error	70	420.62770455	6.00896721		
Corrected Total	79	523.81996875			
		R-Square	C.V.	Root MSE	TSH Mean
		0.196999	30.16777	2.45131948	8.12562500
Source	DF	Type I SS	Mean Square	F Value	Pr > F
DURATION	1	60.27841875	60.27841875	10.03	0.0023
TRT	4	24.87706966	6.21926741	1.03	0.3954
DURATION*TRT	4	18.03677580	4.50919395	0.75	0.5611
Source	DF	Type III SS	Mean Square	F Value	Pr > F
DURATION	1	62.45003165	62.45003165	10.39	0.0019
TRT	4	16.68074247	4.17018562	0.69	0.5986
DURATION*TRT	4	18.03677580	4.50919395	0.75	0.5611

1

MOUSE IMMUNOTOX THYROID HORMONE DATA 22:30 Sunday, October 18, 1998 21
PROC GLM - COLLAPSED ACROSS STUDIES

----- DURATION=14 -----

General Linear Models Procedure
Class Level Information

Class	Levels	Values
TRT	5	0.1-mg/k 1.0-mg/k 3.0-mg/k 30.0-mg/ Control

Number of observations in by group = 150

Group	Obs	Dependent Variables
0	0	TSH
1	150	T4

NOTE: Variables in each group are consistent with respect to the presence or absence of missing values.

1 MOUSE IMMUNOTOX THYROID HORMONE DATA 22:30 Sunday, October 18, 1998 22
 PROC GLM - COLLAPSED ACROSS STUDIES

----- DURATION=14 -----

General Linear Models Procedure

Dependent Variable: T4

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	4	5.77210000	1.44302500	4.86	0.0010
Error	145	43.07150000	0.29704483		
Corrected Total	149	48.84360000			
		R-Square	C.V.	Root MSE	T4 Mean
		0.118175	16.63670	0.54501819	3.27600000
Source	DF	Type I SS	Mean Square	F Value	Pr > F
TRT	4	5.77210000	1.44302500	4.86	0.0010
Source	DF	Type III SS	Mean Square	F Value	Pr > F
TRT	4	5.77210000	1.44302500	4.86	0.0010

1

MOUSE IMMUNOTOX THYROID HORMONE DATA 22:30 Sunday, October 18, 1998 23
PROC GLM - COLLAPSED ACROSS STUDIES

----- DURATION=14 -----

General Linear Models Procedure

Tukey's Studentized Range (HSD) Test for variable: T4

NOTE: This test controls the type I experimentwise error rate, but generally has a higher type II error rate than REGWQ.

Alpha= 0.05 df= 145 MSE= 0.297045
Critical Value of Studentized Range= 3.907
Minimum Significant Difference= 0.3887

Means with the same letter are not significantly different.

Tukey Grouping	Mean	N	TRT
A	3.4633	30	1.0-mg/k
A	3.3883	30	Control
A	3.3283	30	0.1-mg/k
A	3.3000	30	3.0-mg/k
B	2.9000	30	30.0-mg/

1

MOUSE IMMUNOTOX THYROID HORMONE DATA

22:30 Sunday, October 18, 1998 24

PROC GLM - COLLAPSED ACROSS STUDIES

----- DURATION=90 -----

General Linear Models Procedure
Class Level Information

Class	Levels	Values
TRT	5	0.1-mg/k 1.0-mg/k 3.0-mg/k 30.0-mg/ Control

Number of observations in by group = 60

Group	Obs	Dependent Variables
1	58	T4
2	50	TSH

NOTE: Variables in each group are consistent with respect to the presence or absence of missing values.

1

MOUSE IMMUNOTOX THYROID HORMONE DATA
PROC GLM - COLLAPSED ACROSS STUDIES

22:30 Sunday, October 18, 1998 25

----- DURATION=90 -----

General Linear Models Procedure

Dependent Variable: T4

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	4	8.63931034	2.15982759	8.40	0.0001
Error	53	13.62500000	0.25707547		
Corrected Total	57	22.26431034			
		R-Square	C.V.	Root MSE	T4 Mean
		0.388034	17.20744	0.50702611	2.94655172
Source	DF	Type I SS	Mean Square	F Value	Pr > F
TRT	4	8.63931034	2.15982759	8.40	0.0001
Source	DF	Type III SS	Mean Square	F Value	Pr > F
TRT	4	8.63931034	2.15982759	8.40	0.0001

1 MOUSE IMMUNOTOX THYROID HORMONE DATA 22:30 Sunday, October 18, 1998 26
PROC GLM - COLLAPSED ACROSS STUDIES

----- DURATION=90 -----

General Linear Models Procedure

Tukey's Studentized Range (HSD) Test for variable: T4

NOTE: This test controls the type I experimentwise error rate, but generally has a higher type II error rate than REGWQ.

Alpha= 0.05 df= 53 MSE= 0.257075
Critical Value of Studentized Range= 3.994
Minimum Significant Difference= 0.5961
WARNING: Cell sizes are not equal.
Harmonic Mean of cell sizes= 11.53846

Means with the same letter are not significantly different.

Tukey Grouping		Mean	N	TRT
	A	3.6000	12	Control
	A	3.0167	12	0.1-mg/k
B	A	2.8500	10	1.0-mg/k
B		2.8167	12	3.0-mg/k
B		2.4333	12	30.0-mg/

1

MOUSE IMMUNOTOX THYROID HORMONE DATA

22:30 Sunday, October 18, 1998 27

PROC GLM - COLLAPSED ACROSS STUDIES

----- DURATION=90 -----

General Linear Models Procedure

Dependent Variable: TSH

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	4	38.89084545	9.72271136	1.34	0.2681
Error	45	325.30895455	7.22908788		
Corrected Total	49	364.19980000			
		R-Square	C.V.	Root MSE	TSH Mean
		0.106784	30.56031	2.68869632	8.79800000
Source	DF	Type I SS	Mean Square	F Value	Pr > F
TRT	4	38.89084545	9.72271136	1.34	0.2681
Source	DF	Type III SS	Mean Square	F Value	Pr > F
TRT	4	38.89084545	9.72271136	1.34	0.2681

1

MOUSE IMMUNOTOX THYROID HORMONE DATA

22:30 Sunday, October 18, 1998 28

PROC GLM - COLLAPSED ACROSS STUDIES

----- DURATION=90 -----

General Linear Models Procedure

Tukey's Studentized Range (HSD) Test for variable: TSH

NOTE: This test controls the type I experimentwise error rate, but generally has a higher type II error rate than REGWQ.

Alpha= 0.05 df= 45 MSE= 7.229088
Critical Value of Studentized Range= 4.018
Minimum Significant Difference= 3.4235
WARNING: Cell sizes are not equal.
Harmonic Mean of cell sizes= 9.959759

Means with the same letter are not significantly different.

Tukey Grouping	Mean	N	TRT
A	9.933	9	30.0-mg/
A	9.905	10	Control
A	8.264	11	3.0-mg/k
A	8.060	10	1.0-mg/k
A	7.995	10	0.1-mg/k

1

MOUSE IMMUNOTOX THYROID HORMONE DATA 22:30 Sunday, October 18, 1998 29
PROC GLM - COLLAPSED ACROSS STUDIES

----- DURATION=120 -----

General Linear Models Procedure
Class Level Information

Class	Levels	Values
TRT	5	0.1-mg/k 1.0-mg/k 3.0-mg/k 30.0-mg/ Control

Number of observations in by group = 60

Group	Obs	Dependent Variables
1	60	T4
2	30	TSH

NOTE: Variables in each group are consistent with respect to the presence or absence of missing values.

1 MOUSE IMMUNOTOX THYROID HORMONE DATA 22:30 Sunday, October 18, 1998 30
PROC GLM - COLLAPSED ACROSS STUDIES

----- DURATION=120 -----

General Linear Models Procedure

Dependent Variable: T4

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	4	1.08566667	0.27141667	1.08	0.3732
Error	55	13.76416667	0.25025758		
Corrected Total	59	14.84983333			
		R-Square	C.V.	Root MSE	T4 Mean
		0.073110	15.47986	0.50025751	3.23166667
Source	DF	Type I SS	Mean Square	F Value	Pr > F
TRT	4	1.08566667	0.27141667	1.08	0.3732
Source	DF	Type III SS	Mean Square	F Value	Pr > F
TRT	4	1.08566667	0.27141667	1.08	0.3732

1 MOUSE IMMUNOTOX THYROID HORMONE DATA 22:30 Sunday, October 18, 1998 31
PROC GLM - COLLAPSED ACROSS STUDIES

----- DURATION=120 -----

General Linear Models Procedure

Tukey's Studentized Range (HSD) Test for variable: T4

NOTE: This test controls the type I experimentwise error rate, but generally has a higher type II error rate than REGWQ.

Alpha= 0.05 df= 55 MSE= 0.250258
Critical Value of Studentized Range= 3.989
Minimum Significant Difference= 0.576

Means with the same letter are not significantly different.

Tukey Grouping	Mean	N	TRT
A	3.3917	12	30.0-mg/
A	3.2750	12	Control
A	3.2667	12	0.1-mg/k
A	3.2417	12	1.0-mg/k
A	2.9833	12	3.0-mg/k

1

MOUSE IMMUNOTOX THYROID HORMONE DATA
PROC GLM - COLLAPSED ACROSS STUDIES

22:30 Sunday, October 18, 1998 32

----- DURATION=120 -----

General Linear Models Procedure

Dependent Variable: TSH

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	4	4.02300000	1.00575000	0.26	0.8984
Error	25	95.31875000	3.81275000		
Corrected Total	29	99.34175000			
		R-Square	C.V.	Root MSE	TSH Mean
		0.040497	27.87475	1.95262644	7.00500000
Source	DF	Type I SS	Mean Square	F Value	Pr > F
TRT	4	4.02300000	1.00575000	0.26	0.8984
Source	DF	Type III SS	Mean Square	F Value	Pr > F
TRT	4	4.02300000	1.00575000	0.26	0.8984

1

MOUSE IMMUNOTOX THYROID HORMONE DATA 22:30 Sunday, October 18, 1998 33
PROC GLM - COLLAPSED ACROSS STUDIES

----- DURATION=120 -----

General Linear Models Procedure

Tukey's Studentized Range (HSD) Test for variable: TSH

NOTE: This test controls the type I experimentwise error rate, but generally has a higher type II error rate than REGWQ.

Alpha= 0.05 df= 25 MSE= 3.81275
Critical Value of Studentized Range= 4.153
Minimum Significant Difference= 3.3109

Means with the same letter are not significantly different.

Tukey Grouping	Mean	N	TRT
A	7.650	6	3.0-mg/k
A	7.100	6	Control
A	6.917	6	0.1-mg/k
A	6.792	6	30.0-mg/
A	6.567	6	1.0-mg/k